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HFI-35

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration
Cincinnati District Office

Central Region
6751 Steger Drive
Cincinnati, OH 45237-3097
Telephone: (513) 679-2700

December 9, 1999

Warning Letter
CIN-WL-00-16-0

Certified Mail
Return Receipt Requested

William Sanford, President/CEO
Steris Corporation
5960 Heisley Road
Mentor, Ohio 44060

Dear Mr. Sanford:

We are writing to you because during an inspection of your firm located at the above address by the Food and Drug Administration (FDA) on June 15 through August 5, 1999, our Investigators collected information that revealed serious regulatory problems involving the Steris System 1 Processor (SS1), a liquid chemical sterilizer using peracetic acid (PA) and associated accessories to the sterilizer, Quick Connect Kits (QCKs) and Processing Trays; and the Steris Biological Monitoring Kit for the Steris Process.

Under the Federal Food, Drug, and Cosmetic Act (the Act), these products are considered to be medical devices. The law requires that manufacturers of medical devices conform with the requirements of the Quality System Regulation (QS Regulation) as specified in Title 21, Code of Federal Regulations (CFR), Part 820.

The inspection revealed that your devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for the manufacture, processing, packing, storage or distribution are not in conformance with the requirements of the Quality System Regulation as follows:

Steris Biological Monitoring Kit for the Steris Process

1.) Failure to assure that process parameters and components, and device characteristics are adequately monitored and controlled during production.

The following lots of Biological Indicators (BI's) were used as components in the Steris Biological Monitoring Kit for the Steris Process by your firm even though they were found to be out of specifications for PA D-value using the particular Steris BI specifications (SOP 801030) in place at the time acceptance testing was done:

Lot #	
S53603	32.7 s (PA D-value)
S55104	31.5 s (PA D-value)

From a time period of December 1997 to July 1999 your firm did not require that the BI's used as components in your kit have a specific range for D-value for Steam at 121^0 determined by the vendor (NAmSA). As a result, components (BI's) received from your supplier had steam D-values that varied from 0.06 minutes to 1.3 minutes. None of the BI lots accepted had a D-value of [redacted] to [redacted] minutes as stated in your 510(k) submission to FDA for the BI's used in the Steris Biological Monitoring Kit for the Steris process.

Steris System 1

2.) Failure to establish and maintain procedures for validating the device design for Quick Connect Kits under defined operating conditions on initial production units, lots, or batches, or their equivalents and failure to ensure that devices conform to defined user needs and intended uses and that the testing of production units include testing under actual or simulated use conditions, as required by 21 CFR 820.30(g).

For example, your firm's records for the Quick Connect Kits lacked documentation that the normal usage of endoscopes over their expected lifetime will not affect the endoscopes' ability to be adequately sterilized and that the endoscopes' functionality is not adversely affected.

Additionally, there is no documented evidence that testing one Quick Connect Kit with one particular type of scope assures that the tested Quick Connect Kit can be used with all of the types of scopes in that family. The studies to "validate" the Quick Connect Kits show that the flow of sterilant through the lumens is unaffected. The test is conducted three consecutive times and the Quick Connect Kit is approved for use with that particular scope on which it was tested and any model that falls within that scope-family line.

This appears to be a type of design verification rather than validation. Design validation goes beyond the technical issues of verifying that the design input meets the design output. It is intended to ensure that the product meets user requirements, the operating instructions, and any restrictions on the use of the product.

3.) Failure to establish and maintain procedures for verifying the device design, i.e., that the design verification confirms that the design output meets the design input requirements, as required by 21 CFR 820.30(f).

For example, your firm did not have sufficient evidence in its design documentation to demonstrate that all models of endoscopes approved for use with a particular Quick Connect Kit could be adequately processed in the Steris System 1. Also there is no mechanism in your design control procedures for addressing and comparing design inputs to design outputs.

4.) Failure to establish and maintain procedures for the identification, documentation, and validation or where appropriate verification, review, and approval of design changes before their implementation, as required by 21 CFR 820.30(i). For example, after release of a newly designed Quick Connect Kit, there is no mechanism to assure that design changes made to endoscopes do not impact the sterilization, the performance of the Quick Connect Kit, and any additional previous validation results.

5.) Failure to establish and maintain a design history file for each type of device which contains or references the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the design control requirements.

For example, all input requirements for the Quick Connect Kit, such as human factors, labeling requirements, packaging, and risk analysis are not always documented in the design history file, nor are they reviewed or approved.

6.) Failure to establish and maintain procedures which include a mechanism for addressing incomplete, ambiguous or conflicting device requirements, as required in 21 CFR 820.30(c).

For example, the design-input procedures for the Quick Connect Kits lacked a mechanism for addressing incomplete, ambiguous or conflicting requirements.

7.) Failure to establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the device's design development, as required by 21 CFR 820.30(e).

The design procedures covering design review for the Quick Connect Kits are incomplete, in that a) appropriate stages of review are not identified. For example, the design review is only conducted at the end of the design process just prior to release to manufacturing; b) The Standard Operating Procedures do not ensure comprehensive and systematic design review.

8.) Failure to establish and maintain plans that describe or reference the design and development activities and define responsibility for implementation as required by 21 CFR 820.30(b).

For example, there is no design plan for the Quick Connect Kits. According to the Investigators' report, the Test Contract, written for each Kit developed, is used as a plan to develop and test the kits. The Test Contract is inadequate in that it does not contain sufficient information to be considered a design plan.

9.) Failure to have an adequate complaint handling system.

All devices and their model numbers that are involved in complaints are not usually documented; not all data is collected to support the conclusion in the complaint file; and the root cause and reason not to investigate a complaint is not routinely identified and documented.

The following complaints involving alleged serious injuries contained incomplete documentation and root cause evaluation: Complaint [redacted] dated 6/19/98; Complaint [redacted] dated 11/4/98; Complaint # [redacted] dated 2/12/98; Complaint [redacted] dated 6/19/98; Complaint [redacted] dated 5/1/97 and Complaint [redacted] dated 1/15/99.

21 CFR 803.18 requires manufacturers to establish and maintain MDR event files: these files must include "all documentation of the entity's deliberation and decision making processes used to determine if a device-related death, serious injury, or malfunction was or was not reportable under 21 CFR part 803. Pursuant to 21 CFR 803.50(b)(2) manufacturers are also responsible for conducting and investigating each event, and evaluating the cause of the event.

Additionally, the above-stated inspection revealed that your devices are misbranded within the meaning of Section 502(t)(2) of the Act, in that your firm did not conduct an adequate investigation and/or adequately determine the cause of the following events as required by 21 CFR 803.50(b)(2) and these events should have been reported to FDA as serious injuries or malfunctions likely to cause or contribute to serious injury:

•Complaint # [redacted]-MERSA contamination of Olympus Bronchoscope
A customer ([redacted] reported an Olympus Bronchoscope with a MERSA culture on an inner tube of the device after it had been processed in the Steris System 1 processor. This event should have been reported as a MDR malfunction. There is insufficient information in your firm's complaint file to support your decision that your device did not cause or contribute to the contamination.

• Complaint[redacted]-Patient infected with Staphylococcus
[redacted]claimed that two patients in the facility were infected with Staphylococcus as a result of the use of an instruments/device processed in the Steris System 1. This event should have been reported as an MDR serious injury. There is insufficient information in your firm's complaint file to support your decision that your device did not cause or contribute to the infection.

• Complaint[redacted]-Patients infected with Pseudomonas
[redacted]reported that cross contamination resulted in two patients being contaminated with Pseudomonas after Arthroscopy Instrumentation equipment was used on them that was processed in a Steris System 1 processor. This event should have been reported as MDR serious injuries. There is insufficient information in your firm's complaint file to support your decision that the device did not cause or contribute to the Pseudomonas infections.

• [redacted]-Patient infected with Tuberculosis.
[redacted]reported that Tuberculosis outbreak was believed to have been caused by a bronchoscopy processed in the Steris System 1 processor. This event should have been reported as a MDR serious injury due to user error[1]. Your firm's complaint file indicates that the user thought the event could have been the result of user error in that maybe the user did not hook up the Quick Connect Kits correctly. Your firm determined and informed the user facility that they were using the wrong Quick Connect Kit. Your firm then sent the user the correct Quick Connect Kit and conducted training on the device and its cleaning procedures.

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[1] User Error-is defined in the MDR preamble as "any error made by the person using the device. A user error may be the sole cause or merely contribute to a reportable adverse event. (Comment/Response #31)

FDA needs to be aware of events that are related to user error any time such error may have caused or contributed to a reportable event. By receiving such information FDA can determine whether additional measures are necessary to resolve such problems, for example, relabeling or redesign of the device. (Comment/Response #28)

- Complaint #[redacted]-Olympus Bronchoscope contaminated with Tuberculosis [redacted] alleged that an incident involving an Olympus BF-P20D bronchofiberscope processed in a Steris System 1 processor was the cause of a tubercle bacillus or Tuberculosis contamination in the facility due to improper equipment cleaning. This event should have been reported as a MDR malfunction due to user error. Your firm determined that the user facility received incorrect instruction concerning the use of Steris Quick Connect Kits and the facility was processing the Olympus bronchofiberscope without the biopsy valve. Subsequent testing without the valve indicated reductions in sterilant flow throughout the scope.

- Complaint #[redacted]Olympus Bronchoscope contaminated with Tuberculosis [redacted] reported that a bronchoscope was used on a patient with Tuberculosis and after processing in a Steris System 1 processor it was used on other patients. The Hospital tested the bronchoscope after using it on the other patients and the test identified M. tuberculosis on the scope. This event should have been reported as a MDR malfunction. Although your firm does not have sufficient documentation to conclude that your device did not cause or contribute-you did conclude that the hospital was not properly cleaning the devices.

We request that you provide the FDA with documentation concerning the steps your firm is taking to remedy its MDR deficiencies.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the FDA inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts. Also, no requests for Certificates for Products for Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by The Food and Drug Administration without further notice. Possible actions include, but are not limited to, seizure, injunction, and/or civil penalties.

FDA reviewed the documentation submitted by your firm concerning the changes your firm made to your Mellenium Steam Sterilizer. FDA determined that a 510(k) submission is required. Please include in your response to this Warning Letter a proposed date for which you will submit the 510(k) to the FDA, CDRH, Office of Device Evaluation.

In order to facilitate FDA in making the determination that QS Regulation corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, and to resume export clearance for products manufactured at your facility, we are requesting that you submit to this office on the schedule below, certification by an outside expert consultant that it has conducted an audit of your firm's manufacturing and quality assurance systems relative to the requirements of the device QS Regulation (21 CFR, Part 820).

You should also submit a copy of the consultant's report, and certification by your firm's CEO (if other than yourself) that he or she has reviewed the consultant's report and that your firm has initiated or completed all corrections called for in the report. The attached guidance may be helpful in selecting an appropriate consultant. The initial certifications of audit and corrections and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates: June 1, 2000, June 1, 2001, and June 1, 2002.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed.

We received your letters of response to the Form FDA 483 issued to management at your firm at the close of the FDA inspection of your firm on August 5, 1999. The letters were dated August 16, 1999 and August 27, 1999. The corrective actions you indicated you have taken were not adequate to correct all of the deficiencies pointed out to you. We are prepared to meet with you and/or your staff to discuss and/or clarify any of the issues discussed in this Warning Letter and the Form FDA 483.

Your response to this Warning Letter should be sent to Evelyn D. Forney, Compliance Officer, Food and Drug Administration, 6751 Steger Road, Cincinnati, Ohio 45237.

Sincerely,

Mary A Womack for
Henry L. Fielden
District Director
Cincinnati District

Enclosure